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Polyarthritis Associated With Breast Carcinoma

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POLYARTHRITIS HAS BEEN REPORTED to be associated with various types of carcinoma.[1-9] When the primary tumor tissues were removed, the arthritis resolved. Arthritis associated with breast carcinoma was mentioned by MacKenzie and Scherbel,[3] who did not, however, describe the nature and extent of the arthritis. Recently, monarthritis caused by metastatic breast carcinoma was reported by Moutsopoulos and co-workers.[7] We report the case of a patient with breast carcinoma associated with polyarthritis and acute inflammation of the synovial fluid. When the primary tumor was removed, the arthritis resolved within a week.

Report of a Case

A 44-year-old East Indian woman without a history of arthritis was admitted to hospital with a temperature of 37.9°C (100.2°F), malaise and severe incapacitating pain at the right hip and both knees and ankles for three days. A week before the onset of arthritis, she had a needle biopsy of a breast nodule.

At the time she was admitted to hospital, findings on physical examination included a sinus tachycardia of 120 beats per minute with a grade 1 of 6 systolic ejection murmur and a 1.5-cm firm, mobile nodule in the left breast. Tenderness and pain with range of motion were elicited at the right hip. Active synovitis with pain, tenderness, warmth, erythema and moderate swelling was observed at both knees and ankles. Laboratory findings were as follows: a leukocyte count of 11,300 per cu mm with no left shift, a hematocrit of 38 percent and an erythrocyte sedimentation rate (Westergren method) of 90 mm per hr (repeat testing showed 148 mm per hr). The results of electrolyte, liver function, rheumatoid factor and antinuclear antibody (ANA) tests were all normal. Analysis of knee aspirate gave the following values: leukocyte count, 65,000 per cu mm, with 94 percent polymorphonuclear leukocytes; glucose, 111 mg per dl; protein, 5 grams per dl; C_3, 81 mg per dl; no crystals; negative findings on acid-fast smear, and negative cultures for *Neisseria gonorrhoeae* and *Brucella* sp. Cultures of specimens from throat and cervix showed normal flora; the results of blood cultures were negative. The patient was given penicillin and nafcillin intravenously but continued to have temperatures up to 39.6°C (103.3°F) with nausea and vomiting. No apparent improvement occurred in her joint symptoms, and antibiotic therapy was discontinued. The fever abated, however, and she was discharged on a regimen of indomethacin.

The joint symptoms lessened slightly during the next few weeks, then recurred. Active synovitis with symmetric distribution now affected the proximal interphalangeal joints, metacarpophalangeal joints, wrists, elbows, knees and ankles. X-ray films of the sacroiliac joint and hips were normal. She was treated with naproxen and given an intramuscular injection of dexamethasone; her condition improved moderately. The biopsy specimen of the breast nodule showed medullary carcinoma, for which mastectomy was carried out. No lymph node involvement was found. Naproxen therapy was discontinued postoperatively. Three days after the operation, her joint symptoms de-

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creased considerably; by the seventh postoperative day, all joint symptoms had resolved. At multiple follow-up visits over the next 12 months, the patient showed no evidence of arthritis.

Discussion

Various musculoskeletal symptoms have been described as the presenting features of an underlying malignant condition. These symptoms, ranging from myalgia and arthralgia to clinically evident monarthritis or polyarthritis, all resolve when the primary tumor is removed. In our patient, a rapid and disabling polyarthritis developed, which was only partially controlled with nonsteroidal antiinflammatory drugs. When a breast tumor was removed, the arthritis resolved within a week.

The data in the literature on synovial fluid analysis in patients with a malignant lesion have been sparse. Noninflammatory fluid has been described by Ropes and Bauer[10] in patients with pulmonary hypertrophic osteoarthropathy and in the patients reported by Moutsopoulos and associates.[7] In our patient, analysis of a specimen of the synovial fluid from the knee showed an acute inflammatory reaction. Zacharski and Kyle[11] reported that the erythrocyte sedimentation rate was greatly elevated (more than 100 mm an hour, Westergren method) in patients with malignancy. In our patient, the erythrocyte sedimentation rate was elevated to 148 mm per hour (Westergren method).

The pathogenesis of arthritis in association with malignancy is unknown. Husain and colleagues[12] showed a positive result on ANA test to be associated with carcinoma. Sheon and associates[13] reported a positive rheumatoid factor in 27 percent of patients with malignancy. In Bartfeld's[14] survey the incidence of positive rheumatoid factor in patients with malignancy ranged from 1 percent to 20 percent. Circulating immune complexes and hypocomplementemia in patients with carcinoma were reported by Teshima and co-workers[15] and by Rosen and colleagues.[16] Recently, the prostaglandin E_2 (PGE_2) level was shown to increase in patients with metastatic bone disease.[17,18] Pretreatment with administration of indomethacin reduces the amount of PGE_2 extractable from the tumor, as has been proved by Galasko[19] and by Voelkel and associates.[20] Bennett and co-workers[21] and Easty and Easty[22] separately found an increased level of PGE_2 in breast carcinoma tissues. This finding was recently confirmed by Rolland and colleagues.[23] Prostaglandin E_2 is known to be one of the mediators of inflammation. Whether this local increase in PGE_2 relates causally or temporally to the development of arthritis needs further investigation.

Summary

Polyarthritis associated with several types of carcinoma has been reported. We report the case of a patient with breast carcinoma in whom polyarthritis resolved when the tumor was removed. An increase of the amount of prostaglandin E_2 in breast carcinoma tissue, which has been reported in the literature, might be related to the development of arthritis.

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